

Influenza Antivirals

Uses

State's Responsibility

Appropriate Use of Antivirals during a Influenza Pandemic may:

- Reduce morbidity and mortality
- Diminish Overwhelming Demands on Healthcare System
- Contain Small Disease Clusters
 - potentially slow the spread of novel influenza viruses

What is a Pandemic?

A Pandemic occurs when a novel influenza virus emerges that can infect humans and be efficiently transmitted from person to person.

- Infect Humans easily
- Transmitted easily person-to-person
- Could be ANY influenza virus
- Currently worried about Avian Influenza

Do we currently have a Pandemic?

NO

- Avian Influenza is poorly transmitted birds to humans
- Almost never is it transmitted person-to-person

Drugs w/Activity against flu viruses

- M2 ion channel inhibitors (amantadanes)
 - Amantadine (Symmetrel)
 - Rimantadine (Flumadine)
 - **Currently NOT recommended for ANY flu in US**
- Neuraminidases Inhibitors
 - Oseltamivir (Tamiflu)
 - Zanamivir (Relenza)

Uses of Antivirals

- Treatment
- Prophylaxis
- Containment of Disease Clusters

Antivirals for Disease Treatment

Use for H5N1 Avian Influenza

- Neuraminidase Inhibitors (Tamiflu/Relenza) preferred because most H5N1 flu is resistant to amantadine/rimantadine
- Start as quickly as possible – ideally within 48 hours after onset of symptoms (less effective afterwards)
- Can decrease length of infection (1-2 days) and severity IF started w/i 48 hours of onset

Priority Groups for Treatment

- Any person with a potentially life-threatening influenza-related illness
- Any person at high risk for serious complications of influenza and who is within the first 2 days of illness onset

Depending on the severity of the influenza, the above two groups may include many people

How much Antiviral is needed for Treatment?

- **Tamiflu**
 - **75 mg tablet given twice daily**
 - **Given for 5 days or a total of 10 tablets**
 - **Side effects: nausea & vomiting**
 - **Reduced dosage with reduced renal function**
- **Relenza**
 - **Indicated only for those older than 7 y/o**
 - **10 mg inhaled twice daily x 5 days**
 - **Side effects: Bronchospasm**

PROPHYLAXIS

- Is it necessary & feasible to trace a patient's close contacts & provide them with post-exposure antiviral prophylaxis?
- Close Contacts: family, schoolmates, workmates, healthcare providers, fellow passengers (if traveled recently)
- 70%-90% effective in preventing symptoms
- **ONLY** Tamiflu – Relenza currently not indicated for prophylaxis

How much Antiviral is Needed for Prophylaxis

- ONLY Tamiflu
- 75 mg tablet once daily for 7 days after exposure
- Given daily until Institutional Outbreak over
- For 2 weeks if given after vaccine
- Reduced dose for decreased renal function

Contain Small Disease Clusters

- Possibility of halting an early, limited, isolated outbreak (small community or military base)
- After first few cases prophylaxis *everyone* in area (like ring immunization with smallpox)
- Requires rapid delivery
- Uses huge amounts of antivirals
- Once pandemic underway, inefficient use of limited antiviral supplies

Is there Enough Antivirals?

- In a severe Pandemic? – No
- Hence, the need of Government to become involved.
 - **Must plan response BEFORE the pandemic**
 - **Must implement plan early in pandemic**

Projected use of Antivirals in AZ During an Influenza Pandemic

- 75% of hospitalized patients get treated
- 25% of select priority groups would get infected and need treatment
- AZ has roughly 2% of US population
- 2 million people in US may need Post Exposure Prophylaxis (PEP); 2% of that = 40,000
- Prophylaxis requires 4x treatment dose (20 days or 40 tablets) for select priority groups

Projected use of Antivirals in AZ During and Influenza Pandemic

Arizonans who would receive Antivirals

Treatment	775,500	13.2%	6.6 mil pills
Prophylaxis	<u>. 490,000</u>	<u>8.5%</u>	<u>15.1 mil pills</u>
Treatment/Prophy	1,265,500	21.7%	21.7 mil pills

□ 2003 approx. 15 mil doses of Tamiflu used in US

Plans for Prior to Pandemic

- Distribution & use of antivirals during pandemic
- State can broker use of limited supplies
- Request antivirals from Strategic National Stockpile
- Plans for monitoring use
- Procure a supply for use in special populations
- Educate providers about recognizing novel influenza and use of antivirals

Plans for during Pandemic

- Activate plans for distributing/administering antivirals to persons in priority groups
- Review and modify plans as necessary
- Train on appropriate use of antivirals with public health staff & healthcare partners
- Monitor use, effectiveness, adverse events

Plans for during Pandemic

- Ensure effective communication w/public
- Coordinate w/border groups (tribes/counties/Mexico/adjoining States)
- Legal Preparedness
- Contingency for IND use

Plans for during Pandemic Procurement

- Only Tamiflu/Relenza for treatment & ONLY Tamiflu for prophylaxis
- SNS will likely be woefully inadequate (need 22 million doses)
- Must Procure own State Stockpile
- Must manage vendors, storage, distribution
- Encourage hospitals to have own stockpile

Plans for during Pandemic Distribution

- How/where/when to distribute
- Assess and track stocks (hospital/state/SNS)
- Distribute by priority needs
- Establish authority for standing orders at Health Department level (state/local)
- How much for treatment and for prophylaxis
- Broker antiviral supply

Plans for during Pandemic

Priority for Treatment

- Pts admitted to hospital & seriously ill
- HCWs w/direct patient care and EMS
- Highest Risk: Pregnant women, Immuno-compromised
- Health Responders: Public Safety, Government Decision makers
- Increased Risk: Very old and very young and those with underlying medical conditions

Plans for during Pandemic

Priority for Prophylaxis

- HCWs in ERs, ICU, EMS, dialysis centers
- Societal responders & HCWs without direct patient contact (maintain health and a functioning society)
- Other Outpatients who develop influenza and d/n fit into other groups
- Highest Risk Outpatients
- Other HCWs with direct patient care

Plans for during Pandemic

Review and modify plans as necessary

- ADHS will establish a Vaccine and Antiviral Prioritization Advisory Committee
- Multi-disciplinary with representatives from Health Department, EMS, Med Assoc, etc.
- Look at current situation
- Are current needs met by prior plans?
- Recommend changes

Plans for during Pandemic Training

- Work with local health departments, tribal governments, Mexico to enhance training and education
- Clinician Fact Sheets to give valuable information on antiviral use and influenza
- Provide lectures to providers

Plans for during Pandemic

Monitor Use & Collect Data

- Track distribution and use
- Is it effective? Compare treatment/non-treatment groups
- What adverse events are being reported (FDA's Adverse Event Reporting System)
- Evidence of drug resistance to antivirals?
- Is influenza properly diagnosed (tests, etc)

Plans for during Pandemic Public Communication

- Educate public, medical community, stake holders on:
 - Role of Antivirals in responding to pandemic
 - Need to prioritize use of limited antiviral supplies to treatment and prophylaxis
 - Rationale for priority groups identified
 - Importance of appropriate use (as prescribed and for full number of days) to prevent drug resistance
- Information will be provided also in Spanish

Plans for during Pandemic

Coordinate w/border groups

- Includes Mexico, Tribal Groups, adjoining States
- Make certain that plans for educating the public, medical community, stake holders is consistent in all areas

Plans for during Pandemic Legal Preparedness

- During a State of Emergency from a pandemic disease, the Governor may issue orders that ration medicines and vaccines and provide for their procurement
- ADHS will plan for:
 - **Ways for blanket prescriptions for antivirals**
 - **How worker's comp. laws apply**
 - **Coverage of malpractice/tort laws**

Plans for during Pandemic

Plans for Investigational New Drugs

- INDs require:
 - **Strict Inventory Control and record keeping**
 - **Signed Consent Form from *each* patient**
 - **Mandatory Reporting of Certain Adverse Events**
 - **Approval by an Institutional Review Board (IRB)**
- FDA regs allow for national or central IRB for INDs likely to be used in a pandemic
- HHS may provide Emergency Use Authorizations for certain drugs

Will there be enough Antivirals?

- If a Pandemic comes in 10+ years – maybe
- If a Pandemic comes in 1-4 years – most likely not